REMARKS

This Amendment, filed in reply to the Office Action dated August 4, 2008, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 1-11 are withdrawn from consideration as being directed to non-elected inventions. Claims 12-21 are rejected. Claims 12 and 13 are canceled herewith without prejudice or disclaimer. The dependency of Claim 15 is amended herewith in view of the cancellation of Claims 12 and 13. Claim 18 is amended herewith to be dependent from Claim 15. Claim 19 is amended herewith solely to improve clarity. No new matter is added by way of this amendment. Entry and consideration of this amendment are respectfully requested.

Priority

Applicants thank the Examiner for acknowledging Applicants' claim for foreign priority, and receipt of certified copies of all the priority documents.

Information Disclosure Statement

Applicants thank the Examiner for returning a signed and initialed copy of the PTO Form SB/08 that accompanied the Information Disclosure Statement filed March 29, 2006, indicating consideration of the references therein.

The Rejection of Claims 16-19, for Indefiniteness, is Moot

On page 2 of the Office Action, Claims 16-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Specifically, the Examiner asserts that recitation of "the glycine concentration ..." in Claim 16 fails to find proper antecedent basis in Claim 13. Similarly, the Examiner asserts that recitation of "the citric acid ..." in Claims 17 and 18 fails to find proper antecedent basis in Claim 12.

Regarding Claim 19, the Examiner contends that insufficient antecedent basis exists for recitation of "the pH of the solution."

Initially, Applicants note that Claims 12 and 13 are canceled herewith, without prejudice or disclaimer, and Claim 15 has been amended accordingly to depend only from Claim 14, thus mooting the rejection of Claims 16-18. Claims 16-18 as presented ultimately depend from Claim 14, which recites a composition comprising glycine and citric acid.

Regarding Claim 19, while Applicants believe that the scope of this claim would be readily ascertainable by one of skill in the art, in the interest of compacting prosecution, and without acquiescing in the rejection, Applicants herewith amend Claim 19 to recite "wherein said preparation has a pH of between 4 and 7." Applicants respectfully submit that the amendment overcomes the rejection.

Withdrawal of the indefiniteness rejections is respectfully requested.

The Rejection of Claims 12, 13 and 15-20 Under 35 U.S.C. § 102, is Moot

1. On page 3 of the Office Action, Claims 12, 15 and 16 appear to be rejected under 35 U.S.C. 102(a) and (e) as being anticipated by U.S. Application Publication No. 2003/019316 (hereinafter "the '316 publication"), as evidenced by glycine MSDS (Mallinckroadt Chemicals, 2005, p. 1-6).

In making the rejection, the Examiner asserts that the '316 publication discloses an antibody formulation comprising an antibody in a glycine concentration of 0.2M (which is asserted to be 15mg/ml), and wherein the antibody concentration is about 2mg/ml, citing Example 4-5, Figure 13 and Claims 1-6.

The Examiner takes the position that suppressing formation of soluble association of an antibody is an inherent property of glycine. Further, the Examiner contends that the '316 publication discloses that such a composition comprising glycine is more stable because it reduces aggregation, citing paragraph [0089].

Initially, Applicants note that Claim 12 is canceled herewith, mooting the rejection of this claim. Regarding Claims 15 and 16, Applicants note that these claims as presented ultimately depend only from Claim 14, which recites a composition comprising glycine and citric acid. Because Claim 14 is not anticipated by the '316 publication, as acknowledged by the Examiner, Claims 15 and 16 as presented are also not anticipated by the '316 publication, at least by virtue of their dependency on Claim 14. In addition, Applicants note that the '316 publication neither teaches nor reasonably suggests a composition comprising citric acid. Accordingly, the '316 publication does not teach each and every element of Claims 15 or 16, as is required to maintain an anticipation rejection.

Withdrawal of the rejection is respectfully requested.

2. On page 4 of the Office Action, Claims 13, 15 and 17-20 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/37329 (hereinafter "the '329 publication").

In making the rejection, the Examiner asserts that the '329 publication discloses an isotonic antibody composition comprising citrate at a concentration of 5-20mmol/L, and wherein

the antibody concentration is between 0.5-10mg/ml, citing Claims 1-9. The Examiner further asserts that the '329 publication discloses addition of polysorbate 80, a non-ionic surfactant. The Examiner takes the position that suppressing formation of a chemically degraded product of an antibody is an inherent property of citrate.

Initially, Applicants note that Claim 13 is canceled herewith, mooting the rejection of this claim. Regarding Claims 15 and 17-20, Applicants note that these claims as presented ultimately depend only from Claim 14, which recites a composition comprising glycine and citric acid. Because Claim 14 is not anticipated by the '329 publication, as acknowledged by the Examiner, Claims 15 and 17-20 as presented are also not anticipated by the '329 publication, at least by virtue of their dependency on Claim 14. In addition, Applicants note that the '329 publication neither teaches nor reasonably suggests a composition comprising glycine. Accordingly, the '329 publication does not teach each and every element of Claims 15 and 17-20, as is required to maintain an anticipation rejection.

Withdrawal of the rejection is respectfully requested.

Claims 14-21 are Patentable Under 35 U.S.C. § 103(a)

1. On page 5 of the Office Action, Claims 14-20 are rejected under 35 U.S.C. 103 as being unpatentable over WO 99/37329 (i.e. "the '329 publication") in view of U.S. 2003/019316 (i.e., "the '316 publication").

The '329 publication is relied upon for the same reasons as discussed above in the rejection of Claims 13, 15 and 17-20 under 35 U.S.C. 102(b). However, the Examiner acknowledges that the '329 publication does not disclose an antibody composition containing glycine.

In an attempt to rectify the deficiencies of the '329 publication, the Examiner cites to the '316 publication, which allegedly discloses that the addition of glycine to an antibody composition improves stability by reducing aggregation, citing paragraph [0089].

The Examiner contends that one of ordinary skill in the art at the time the invention was made would readily have added glycine, as taught by the '316 publication, to the antibody formulation taught by the '329 publication to improve the stability of the antibody formulation by reducing aggregation.

Applicants respectfully disagree, and traverse the rejection on the following grounds.

Applicants respectfully submit that the instantly claimed invention is not rendered obvious by the cited references at least because the cited references teach away from the claimed composition.

Specifically, one of ordinary skill in the art would be discouraged from producing the claimed composition in view of the '329 publication because the '329 publication teaches away from the inclusion of other stabilization agents, such that one of ordinary skill in the art would have no motivation, nor any expectation of success in improving stability of an antibody formulation, by adding glycine to the composition of the '329 publication. For example, on page 2, lines 27-29, of the '329 publication, it is disclosed that the composition preferably is free of <u>any</u> additional compound known for use in antibody stabilization, such as Tween, mannitol or maltose. Further, one of ordinary skill in the art would also be discouraged from producing the claimed composition in view of the experimental data disclosed in the '329 publication. On page 9 of the '329 publication, it is disclosed that "the formulations exemplified in examples 1-7 were stable for <u>24 months</u> whereas the formulation in example 8 was stable for <u>12 months</u>." (Emphasis added.) Applicants point out that the formulation in example 8 is identical to the formulation

used in example 1, except that the formulation in example 8 also contains a further stabilizing agent, namely polysorbate 80 (i.e., Tween-80). Accordingly, one of ordinary skill in the art would readily understand from the '329 publication that the inclusion of an additional art-recognized stabilizing agent in the citric acid buffer of the '329 publication, rather than further enhancing the stability of the antibody in the citrate buffer, actually has the *opposite* effect, in that it *reduces* the stability of the antibody in the citrate buffer (from 24 months to 12 months). Accordingly, one of ordinary skill in the art would have no motivation to add additional stabilizing agents to the citrate buffer of the '329 publication, because the '329 publication teaches away from the addition of further protein stabilizing agents by demonstrating that the addition of Tween-80 (an art-recognized protein stabilizing agent), rather than increasing antibody stability, actually *decreases* antibody stability. It is well-settled that a reference teaches away when a person of ordinary skill in the art, upon reading it, would be discouraged from following the path set out in the reference, or would be led in a path divergent from the path taken by the inventor. See *Monarch Knitting Mach. Corp v. Sulzer Morat Gmbh*, 139 F.3d, 877, 45 USPQ2d 1977 (Fed. Cir. 1998); *Para-Ordnance Mfg. v. SGS Importers Int'l Inc.*, 73 F.3d1085, 37 USPQ2d 1237 (Fed. Cir. 1995); and *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994). Clearly, one of ordinary skill in the art, reading the '329 publication, would be discouraged from including additional protein stabilizing agents in an antibody composition stabilized with citric acid, because the '329 publication teaches that the citric composition should be free of other protein-stabilizing agents, and because the '329 publication also experimentally demonstrates that the addition of Tween-80, an art-recognized protein stabilizing agent, severely *inhibits* the stabilizing effect of citric acid.

For the foregoing reasons, the instant claims are not rendered obvious by the cited references.

Withdrawal of the rejection is respectfully requested.

2. On page 6 of the Office Action, Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/37329 (i.e., the '329 publication) in view of U.S. Patent Application Publication No. 2003/019316 (i.e., the '316 publication) as applied to Claims 14-20 above, and further in view of U.S. Patent No. 6,488,930 (hereinafter "the '930 Patent").

The '316 and '329 publications are relied upon for the same reasons as discussed above in the rejection of Claims 14-20 under 35 U.S.C. 103(a). However, the Examiner acknowledges that neither publication discloses a humanized antibody to CCR4.

In an attempt to rectify the deficiencies of the primary references, the Examiner cites to the '930 Patent, which allegedly discloses a composition comprising a humanized CCR4 antibody (citing Claims 6 and 47).

From the above references, the Examiner contends that it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a stabilizing composition containing glycine and citric acid, "as taught by the '316 publication and the '329 publication," to stabilize a CCR4 humanized antibody, as disclosed by the '930 Patent. The Examiner asserts that one of ordinary skill in the art would have been motivated to do so because the formulations taught by the '316 and the '329 publications improve antibody stability.

Applicants respectfully submit that Claim 21 is not rendered obvious for the same reasons as discussed above for Claims 14-20.

Withdrawal of the rejection is respectfully requested.

3. On page 6 of the Office Action, Claim 21 is further rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/37329 (i.e., the '329 publication) in view of U.S. Patent Application Publication No. 2003/019316 (i.e., the '316 publication) as applied to Claims 14-20 above, and further in view of U.S. Patent No. 6,437,098 (hereinafter "the '098 Patent").

The '316 and '329 publications are relied upon for the same reasons as discussed above in the rejection of Claims 14-20 under 35 U.S.C. 103(a). However, the Examiner acknowledges that neither publication discloses a humanized antibody to GD3.

In an attempt to rectify the deficiencies of the primary references, the Examiner cites to the '098 Patent, which allegedly discloses a humanized GD3 antibody (citing Claims 1 and 2).

From the above references, the Examiner contends that it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a stabilizing composition containing glycine and citric acid, "as taught by the '316 publication and the '329 publication," to stabilize a GD3 humanized antibody, as disclosed by the '098 Patent. The Examiner asserts that one of ordinary skill in the art would have been motivated to do so because the formulations taught by the '316 and the '329 publications improve antibody stability.

Applicants respectfully submit that Claim 21 is not rendered obvious for the same reasons as discussed above for Claims 14-20.

Withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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Date: November 4, 2008